

## 5 **CLAIMS**

1. An altered antibody or functional fragment thereof which binds to and neutralises MAG and which comprises one or more of the following CDR's.

### 10 ***Light chain CDRs***

<b><i>CDR</i></b>	<b><i>According to Kabat</i></b>
L1	KSSHSLYSSNQKNYLA
L2	WASTRES
L3	HQYLSSLT

### ***Heavy chain CDRs***

<b><i>CDR</i></b>	<b><i>According to Kabat</i></b>
H1	NYGMN
H2	WINTYTGEPTYADDFTG
H3	NPINYYGINYEGYVMDY

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2. An altered antibody or functional fragment thereof which comprises a heavy chain variable domain which comprises one or more CDR's selected from CDRH1, CDRH2 and CDRH3 and/or a light chain variable domain which comprises one or more CDRs selected from CDRL1, CDRL2 and CDRL3 .

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3. An altered anti-Mag antibody or functional fragment thereof which comprises:

a heavy chain variable domain ( $V_H$ ) which comprises in sequence hypervariable regions CDRH1, CDRH2 and CDRH3 and /or

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- 5 a light chain variable domain ( $V_L$ ) which comprises in sequence hypervariable regions CDRL1, CDRL2 and CDRL3.
4. An antibody of claim 3 which is monoclonal.
- 10 5. An antibody of claim 4 which is humanised.
6. An antibody or functional fragment thereof that according to claim 5 which comprises a heavy chain variable region comprising one of the following amino acid sequences
- 15 QVQLVQSGSELKKPGASVKVSCASGYTFTNYGMNWVRQAPGQGLEWMGWI  
NTYTGEPTYADDFTGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARNPIN  
YGINYEGYVMDYWGQGTLVTVSS (SEQ ID No 13).
- 20 QVQLVQSGSELKKPGASVKVSCASGYTFTNYGMNWVRQAPGQGLEWMGWI  
NTYTGEPTYADDFTGRFVFSLDTSVSTAYLQISSLKAEDTAVYFCARNPIN  
YGINYEGYVMDYWGQGTLVTVSS (Sequence ID No 14)
- 25 QVQLVQSGSELKKPGASVKVSCASGYTFTNYGMNWVRQAPGQGLEWMGWI  
NTYTGEPTYADDFTGRFVFSLDTSVSTAYLQISSLKAEDTATYFCARNPIN  
YGINYEGYVMDYWGQGTLVTVSS (sequence ID No 15)
7. An antibody or functional fragment thereof according to claim 6 further comprising a light chain variable region comprising amino acid Sequence
- 30 ID No 16, 17, 18 or 19:

DIVMTQSPDSLAVSLGERATINCKSSHSVLYSSNQKNYLAWYQQKPGQPPK  
 LLIYWASTRESGVPDRFSGSGSGTDFTLTIISSLQAEDVAVYYCHQYLSSLT  
 FGQGTKLEIKRTV (SEQ ID No 16)

- 35 DIVMTQSPDSLAVSLGERATINCKSSHSVLYSSNQKNYLAWYQQKPGQPPK  
 LLIYWASTRESGVPDRFSGSGSGTDFTLTIIINLQAEDVAVYYCHQYLSSLT  
 FGQGTKLEIKRTV (SEQ ID No 12)

5 DIVMTQSPDSLAVSLGERATINCKSSHVLYSSNQKNYLAWYQQKPGQPPK  
 LLIYWASTRESGVPDRFSGSGSGTDFTLTITISLHTEDVAVYYCHQYLSSLT  
 FGQGTKLEIKRTV (SEQ ID No 18)

10 DIVMTQSPDSLAVSLGERATINCKSSHVLYSSNQKNYLAWYQQKPGQPPK  
 LLIYWASTRESGVPDRFSGSGSGTDFTLTITINLHTEDVAVYYCHQYLSSLT  
 FGQGTKLEIKRTV (SEQ ID No 19)

8. An antibody according to claims 6 – 7 comprising:  
 a heavy chain variable fragment comprising SEQ ID No 13,14 or 15  
 15 and a constant part or fragment thereof of a human heavy chain  
 and  
 a light chain variable fragment comprising SEQ ID No 16, 17, 18 or 19 and  
 a constant part or fragment thereof of a human light chain.
- 20 9. An humanised antibody according to any preceding claim selected from  
 antibodies comprising:  
 Heavy chain variable region comprising Seq ID No 13 and light chain  
 variable region comprising Seq ID No 16;  
 Heavy chain variable region comprising Seq ID No 13 and light chain  
 25 variable region comprising Seq ID No 17;  
 Heavy chain variable region comprising Seq ID No 13 and light chain  
 variable region comprising Seq ID No 18;  
 Heavy chain variable region comprising Seq ID No 13 and light chain  
 variable region comprising Seq ID No 19.  
 30 Heavy chain variable region comprising Seq ID No 14 and light chain  
 variable region comprising Seq ID No 16;  
 Heavy chain variable region comprising Seq ID No 14 and light chain  
 variable region comprising Seq ID No 17;  
 Heavy chain variable region comprising Seq ID No 14 and light chain  
 35 variable region comprising Seq ID No 18;  
 Heavy chain variable region comprising Seq ID No 14 and light chain  
 variable region comprising Seq ID No 19.

- 5 Heavy chain variable region comprising Seq ID No 15 and light chain variable region comprising Seq ID No 16;  
Heavy chain variable region comprising Seq ID No 15 and light chain variable region comprising Seq ID No 17;  
Heavy chain variable region comprising Seq ID No 15 and light chain variable region comprising Seq ID No 18;  
10 Heavy chain variable region comprising Seq ID No 15 and light chain variable region comprising Seq ID No 19.

10. A polynucleotide encoding the heavy chain variable region comprising  
15 Sequence ID No 15.

20 CAGGTGCAGCTGGTGCAATCTGGGTCTGAGTTGAAGAAGCCTGGGGCCTCA  
GTGAAGGTTTCCTGCAAGGCTTCTGGATACACCTTCACTAACTACGGCATG  
AACTGGGTGCGACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGATGGATC  
AAACACCTACACCGGCGAGCCACCTACGCCGACGACTTCACCGGCCGGTTT  
GTCTTCTCCTTGGACACCTCTGTCAGCACGGCATATCTGCAGATCAGCAGC  
CTAAAGGCTGAGGACACTGCCGTGTATTACTGTGCGAGAAACCCCATCAAC  
TACTACGGCATCAACTACGAGGGCTACGTGATGGACTACTGGGGCCAGGGC  
25 ACAC TAGTCACAGTCTCCTCA

- 25 11. A polynucleotide sequence encoding the amino acid Sequence ID No 14 is:

30 CAGGTGCAGCTGGTGCAATCTGGGTCTGAGTTGAAGAAGCCTGGGGCCTCA  
GTGAAGGTTTCCTGCAAGGCTTCTGGATACACCTTCACTAACTACGGCATG  
AACTGGGTGCGACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGATGGATC  
AAACACCTACACCGGCGAGCCACCTACGCCGACGACTTCACCGGCCGGTTT  
GTCTTCTCCTTGGACACCTCTGTCAGCACGGCATATCTGCAGATCAGCAGC  
CTAAAGGCTGAGGACACTGCCGTGTATTCTGTGCGAGAAACCCCATCAAC  
TACTACGGCATCAACTACGAGGGCTACGTGATGGACTACTGGGGCCAGGGC  
35 ACAC TAGTCACAGTCTCCTCA

- 35 12. A polynucleotide sequence encoding the amino acid Sequence ID No 15 is:

40 CAGGTGCAGCTGGTGCAATCTGGGTCTGAGTTGAAGAAGCCTGGGGCCTCA  
GTGAAGGTTTCCTGCAAGGCTTCTGGATACACCTTCACTAACTACGGCATG  
AACTGGGTGCGACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGATGGATC  
AAACACCTACACCGGCGAGCCACCTACGCCGACGACTTCACCGGCCGGTTT  
GTCTTCTCCTTGGACACCTCTGTCAGCACGGCATATCTGCAGATCAGCAGC

5 CTAAAGGCTGAGGACACTGCCACCTATTTCTGTGCGAGAAACCCCATCAAC  
TACTACGGCATCAACTACGAGGGCTACGTGATGGACTACTGGGGCCAGGGC  
ACACTAGTCACAGTCTCCTCA

10 13 A polynucleotide encoding amino acid Sequence ID No 16 is:

GACATCGTGATGACCCAGTCTCCAGACTCCCTGGCTGTGTCTCTGGGCGAG  
AGGGCCACCATCAACTGCAAGAGCAGCCACAGCGTGCTGTACAGCAGCAAC  
CAGAAGAACTACCTGGCCTGGTACCAGCAGAAACCAGGACAGCCTCCTAAG  
CTGCTCATTTACTTGGGCATCTACCCGGGAATCCGGGGTCCCTGACCGATTCT  
15 AGTGGCAGCGGGTCTGGGACAGATTTCACTCTCACCATCAGCAGCCTGCAG  
GCTGAAGATGTGGCAGTTTATTACTGTACCAGTACCTGAGCAGCCTGACC  
TTTGGCCAGGGGACCAAGCTGGAGATCAAACGTACGGTG

20 14. A polynucleotide sequence encoding amino acid SEQ ID No 17 is:

GACATCGTGATGACCCAGTCTCCAGACTCCCTGGCTGTGTCTCTGGGCGAG  
AGGGCCACCATCAACTGCAAGAGCAGCCACAGCGTGCTGTACAGCAGCAAC  
CAGAAGAACTACCTGGCCTGGTACCAGCAGAAACCAGGACAGCCTCCTAAG  
CTGCTCATTTACTTGGGCATCTACCCGGGAATCCGGGGTCCCTGACCGATTCT  
25 AGTGGCAGCGGGTCTGGGACAGATTTCACTCTCACCATCATCAACCTGCAG  
GCTGAAGATGTGGCAGTTTATTACTGTACCAGTACCTGAGCAGCCTGACC  
TTTGGCCAGGGGACCAAGCTGGAGATCAAACGTACGGTG

30 15. A polynucleotide encoding amino acid SEQ ID No 18 is:

GACATCGTGATGACCCAGTCTCCAGACTCCCTGGCTGTGTCTCTGGGCGAG  
AGGGCCACCATCAACTGCAAGAGCAGCCACAGCGTGCTGTACAGCAGCAAC  
CAGAAGAACTACCTGGCCTGGTACCAGCAGAAACCAGGACAGCCTCCTAAG  
CTGCTCATTTACTTGGGCATCTACCCGGGAATCCGGGGTCCCTGACCGATTCT  
35 AGTGGCAGCGGGTCTGGGACAGATTTCACTCTCACCATCAGCAGCCTGCAC  
ACCGAAGATGTGGCAGTTTATTACTGTACCAGTACCTGAGCAGCCTGACC  
TTTGGCCAGGGGACCAAGCTGGAGATCAAACGTACGGTG

40 16. A polynucleotide encoding amino acid SEQ ID No 15 is:

GACATCGTGATGACCCAGTCTCCAGACTCCCTGGCTGTGTCTCTGGGCGAG  
AGGGCCACCATCAACTGCAAGAGCAGCCACAGCGTGCTGTACAGCAGCAAC  
CAGAAGAACTACCTGGCCTGGTACCAGCAGAAACCAGGACAGCCTCCTAAG  
CTGCTCATTTACTTGGGCATCTACCCGGGAATCCGGGGTCCCTGACCGATTCT  
45 AGTGGCAGCGGGTCTGGGACAGATTTCACTCTCACCATCATCAACCTGCAC  
ACCGAAGATGTGGCAGTTTATTACTGTACCAGTACCTGAGCAGCCTGACC  
TTTGGCCAGGGGACCAAGCTGGAGATCAAACGTACGGTG

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17. A pharmaceutical composition comprising an altered anti-MAG antibody or functional fragment thereof according to claims 1-8 together with a pharmaceutically acceptable diluent or carrier.

10 18. A method of treatment or prophylaxis of stroke and other neurological diseases/disorders in a human which comprises administering to said human in need thereof an effective amount of an anti-MAG antibody, according to claims 1-8 including altered antibodies or a functional fragment thereof.

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19. The use of an anti-MAG antibody according to claims 1-8, including altered antibodies or a functional fragment thereof in the preparation of a medicament for treatment or prophylaxis of stroke and other neurological diseases/disorders.

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20. A method of inhibiting neurodegeneration and/or promoting functional recovery in a human patient suffering, or at risk of developing, a stroke or other neurological disease/disorder which comprises administering to said human in need thereof an effective amount of an anti-MAG antibody according to claims 1-6, including altered antibodies or a functional fragment thereof.

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21. The use of an anti-MAG antibody according to claims 1-8, including altered antibodies or a functional fragment thereof in the preparation of a medicament for inhibiting neurodegeneration and/or promoting functional recovery in a human patient afflicted with, or at risk of developing, a stroke and other neurological disease/disorder.

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- 5     22.     A method of treating or prophylaxis of stroke or other neurological disease/disorder in a human comprising the step of parenteral administration of a therapeutically effective amount of an anti-MAG antibody to said human.
- 10    23.     The method of claim 22 wherein the anti-MAG antibody is administered intravenously.
- 15    24.     The method of claim 18, 20 or 24 wherein the other neurological disease/disorder is selected from the group consisting of; traumatic brain injury, spinal cord, Alzheimer's disease, fronto-temporal dementias (tauopathies), peripheral neuropathy, Parkinson's disease, Huntington's disease and multiple sclerosis.
- 20    25.     A method of promoting axonal sprouting comprising the step of contacting a human axon with an anti-MAG antibody of claims 1 to 8.
26.     The method of claim 25 wherein the method is *in vitro*.